Induced Pluripotent Stem Cell - Derived Mesenchymal Stem Cells: Progress Toward Safe Clinical Products.

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Public Summary:
Gene-modified mesenchymal stem cells can serve as potent delivery vehicles but there are key safety concerns from the use of integrating vectors, which must be considered when moving toward clinical trials. The future use of human embryonic or induced pluripotent stem cells as a source for producing MSCs would allow gene targeting through homologous recombination, or random integration and selection of those pluripotent clones that had the transgene integrated into a "safe harbor" site. The appropriate, selected pluripotent stem cell clones could be expanded greatly prior to differentiation to MSCs. We have demonstrated that human embryonic stem cell - derived MSCs home to sites of ischemia and tissue damage, and behave much like thier adult counterparts. The current manuscript describes progress toward producing functional MSCs from hESC and iPSCs, and the future potential for this field.

Scientific Abstract:
Adult stem cell therapies have provided success for more than 50 years, through reconstitution of the hematopoietic system using bone marrow, umbilical cord blood, and mobilized peripheral blood transplantation. Mesenchymal stem cell (MSC) -mediated therapy is a fast-growing field that has proven safe and effective in the treatment of various degenerative diseases and tissue injuries. Since the first derivations of embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC), there has been impressive progress toward developing safe clinical applications from pluripotent stem cells. Recent successes in transgene-free iPSC reprogramming have brought attention to the potential of clinical applications of these pluripotent cells, but key hurdles must be overcome, which are discussed in this review. Looking to the future, it could be advantageous to derive MSC from iPSC or hESC in cases where genetic engineering is needed, since in the pluripotent stem cells, clones with "safe harbor" vector integration could be selected, expanded and differentiated. Here we describe the status of the progress of the use of MSC and pluripotent stem cells in clinical trials and analyze the challenges that should be overcome before iPSC-derived MSC therapy can be used widely in the clinic.